

Amendments to the Specification:

Please replace the paragraph beginning at page 1, line 3, with the following amended paragraph:

This application is a continuation (and claims the benefit of priority under 35 USC 120) of U.S. application Serial No. 10/749,699, filed December 30, 2003, which is a continuation of U.S. application serial no. Serial No. 09/953,323, filed September 14, 2001 (now abandoned), which claims the benefit of U.S. application Serial No. 60/232,251, filed September 14, 2000 (now expired). The disclosures of the prior applications are considered part of (and are incorporated by reference in) the disclosure of this application.

Please replace the paragraph beginning at page 6, line 2, with the following amended paragraph:

Fig. 1 is a representation of a ~~wild-type~~ mutant IL-15 nucleic acid sequence (SEQ ID NO:1) and the predicted amino acid sequence (SEQ ID NO:2).

Please replace the paragraph beginning at page 6, line 4, with the following amended paragraph:

Fig. 2 is a representation of a ~~mutant~~ wild-type IL-15 nucleic acid sequence (SEQ ID NO:3) and the predicted amino acid sequence (SEQ ID NO:4). The wild-type codon encoding glutamine at position at 149, CAG, and the wild-type codon encoding glutamine at position 156, CAA, ~~have both been~~ are both changed to GAC, which encodes aspartate, in the mutant sequence shown in Fig. 1. (These positions (149 and 156) correspond to positions 101 and 108, respectively, in the mature IL-15 polypeptide, which lacks a 48-amino acid signal sequence).

Please replace the paragraph beginning at page 12, line 8, with the following amended paragraph:

Mutant IL-15 polypeptides that bind the IL-15 receptor complex with an affinity similar to wild-type IL-15, but fail to fully activate signal transduction, have been produced. These mutant polypeptides compete effectively with wild-type IL-15 polypeptides and can inhibit one or more of the events that normally occur in response to IL-15 signaling, such as cellular

proliferation. The "wild-type IL-15 polypeptide" referred to herein is a polypeptide that is identical to a naturally occurring IL-15 (e.g., a wild-type IL-15 polypeptide is shown in Fig. 1 and Fig. 2). In contrast, a "mutant IL-15 polypeptide" is a polypeptide that has at least one mutation relative to wild-type IL-15 and that inhibits at least one of the *in vivo* or *in vitro* activities that are usually promoted by wild-type IL-15.

Please replace the paragraph beginning at page 13, line 11, with the following amended paragraph:

A mutant IL-15 polypeptide of the invention can be at least 65%, preferably at least 80%, more preferably at least 90%, and most preferably at least 95% (e.g., 96%, 97%, 98% or 99%) identical to wild-type IL-15. The mutation can consist of a change in the number or content of amino acid residues. For example, the mutant IL-15 can have a greater or a lesser number of amino acid residues than wild-type IL-15. Alternatively, or in addition, the mutant polypeptide can contain a substitution of one or more amino acid residues that are present in the wild-type IL-15. The mutant IL-15 polypeptide can differ from wild-type IL-15 by the addition, deletion, or substitution of a single amino acid residue, for example, an addition, deletion or substitution of the residue at position 156. Similarly, the mutant polypeptide can differ from wild-type by an addition, deletion, or substitution of two amino acid residues, for example, the residues at positions 156 and 149. For example, the mutant IL-15 polypeptide can differ from wild-type IL-15 by the substitution of aspartate for glutamine at residues 156 and 149 (as shown in Fig. 1). Mutant polypeptides useful as targeting agents, like wild-type IL-15, recognize and bind a component of the IL-15R. In one embodiment, the mutation of IL-15 is in the carboxy-terminal domain of the cytokine, which is believed to bind IL-2R $\gamma$  (the IL-2 receptor subunit). Alternatively, or in addition, mutant IL-15 polypeptides can include one or more mutations within IL-2R $\beta$  (the IL-2 receptor  $\beta$  subunit) binding domain.